

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE United States Patent and Trademark Office Address: COMMISSIONER FOR PATENTS P.O. Box 1450 Alexandria, Virginia 22313-1450 www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO	
08/475,822	06/07/1995	MARC ALIZON	3495.0010-24	4214	
22852	7590 . 02/13/2004		EXAMINER		
FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER			FREDMAN, JEFFREY NORMAN		
LLP 1300 I STREE	T. NW		ART UNIT	PAPER NUMBER	
WASHINGTON, DC 20005			1634		
		DATE MAILED: 02/13/200	4		

Please find below and/or attached an Office communication concerning this application or proceeding.

		Application N	o.	Applicant(s)				
Office Action Summary		08/475,822		ALIZON ET AL.				
		Examin r		Art Unit				
		Jeffrey Fredm		1634				
Period fo	The MAILING DATE of this communication app or Reply	ears on the cov	er sheet with the c	orrespondence ad	ldress			
A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION. - Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication. - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely. - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication. - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). - Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).								
Status								
1) \[\]	Responsive to communication(s) filed on <u>19 November 2003</u> . This action is FINAL . 2b) This action is non-final.							
2a)□	,				a madita ia			
3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under <i>Ex parte Quayle</i> , 1935 C.D. 11, 453 O.G. 213. Disposition of Claims								
·	Claim(s) 35-46 is/are pending in the application	n.						
•,	4a) Of the above claim(s) is/are withdrawn from consideration.							
5)□								
	☐ Claim(s) 35-46 is/are rejected.							
7)	Claim(s) is/are objected to.							
8)□	Claim(s) are subject to restriction and/or	election requi	rement.					
Applicat	ion Papers							
9)[The specification is objected to by the Examiner	r.						
10)	The drawing(s) filed on is/are: a)□ accep	ted or b)☐ obje	cted to by the Exan	niner.				
	Applicant may not request that any objection to the	e drawing(s) be h	eld in abeyance. Se	ee 37 CFR 1.85(a).				
11)	The proposed drawing correction filed on	is: a)□ appro	ved b)⊡ disappro	ved by the Examin	er.			
If approved, corrected drawings are required in reply to this Office action.								
12)☐ The oath or declaration is objected to by the Examiner.								
Priority (under 35 U.S.C. §§ 119 and 120							
13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).								
a)	a) ☐ All b) ☐ Some * c) ☐ None of:							
	1. Certified copies of the priority documents have been received.							
	2. Certified copies of the priority documents have been received in Application No							
* 5	 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)). * See the attached detailed Office action for a list of the certified copies not received. 							
14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).								
a) The translation of the foreign language prov Acknowledgment is made of a claim for domestic	visional applica	ation has been rece	eived.	,			
ر اسارت Attachmen		o priority under						
1) Notice 2) Notice	e of References Cited (PTO-892) e of Draftsperson's Patent Drawing Review (PTO-948) mation Disclosure Statement(s) (PTO-1449) Paper No(s)	4) [5) [6) [Notice of Informal P	(PTO-413) Paper No atent Application (PT				

Application/Control Number: 08/475,822 Page 2

Art Unit: 1634

DETAILED ACTION

Continued Examination Under 37 CFR 1.129(a)

1. Since this application is eligible for the transitional procedure of 37 CFR 1.129(a), and the fee set forth in 37 CFR 1.17(r) has been timely paid, the finality of the previous Office action is hereby withdrawn pursuant to 37 CFR 1.129(a). Applicant's first submission after final filed on November 19, 2003 has been entered.

Claim Objections

2. The numbering of claims is not in accordance with 37 CFR 1.126 which requires that when new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Here, two claims are numbered "41".

Misnumbered claim 41 been renumbered 42. Specifically, the second claim "41", drawn to the kit of claim 41, was renumbered 42.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application

Art Unit: 1634

being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

4. Claims 35, 37, 39, 41, 43 and 45 are rejected under 35 U.S.C. 102(e) as being anticipated by Chang et al (U.S. Patent 6,001,977).

Chang teaches in vitro diagnostic methods for detecting the presence or absence of HIV-1 virus in a biological sample (column 9, lines 25-62) comprising:

contacting said biological sample with a nucleic acid probe of HIV-1 selected from the HIV sequence (column 9, lines 25-62 and column 10, line 65 to column 11, line 32),

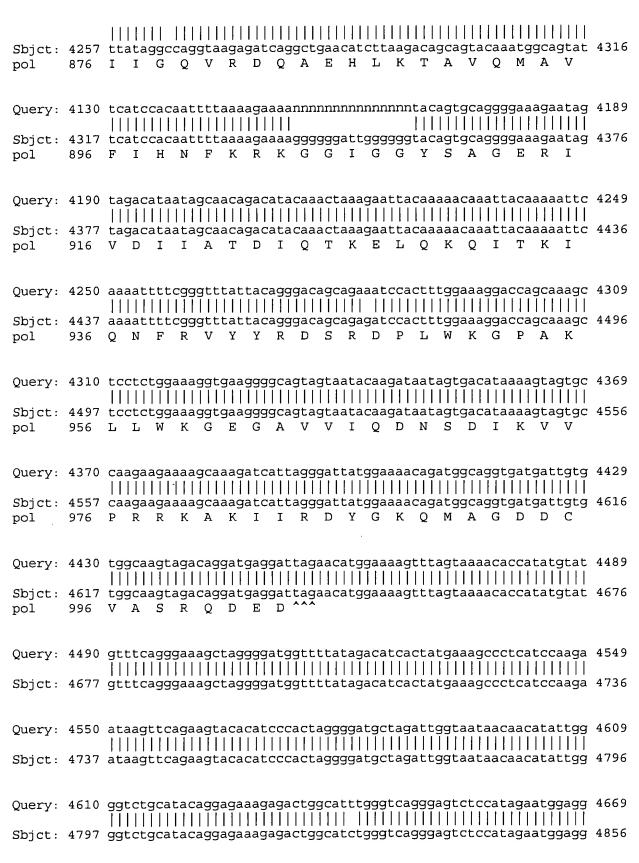
where the specific sequence is disclosed as SEQ ID NO: 4, for example (columns 19-28).

And detecting the formation of hybrids in the biological sample (column 9, lines 25-62).

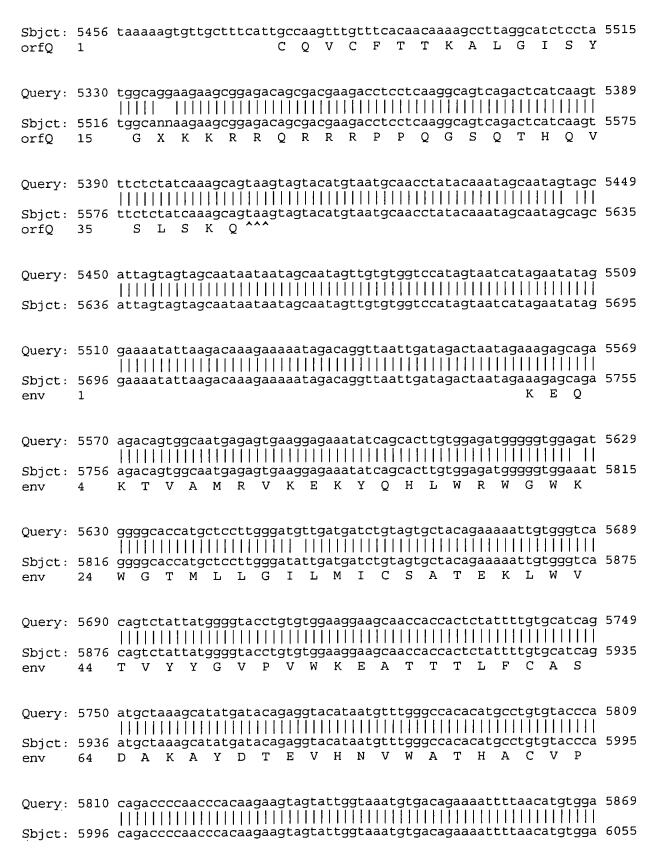
Chang further teaches the compositions of these nucleic acids (column 9, lines 25-62) as well as HTLV-I and II negative control sequences (column 9, lines 25-62).

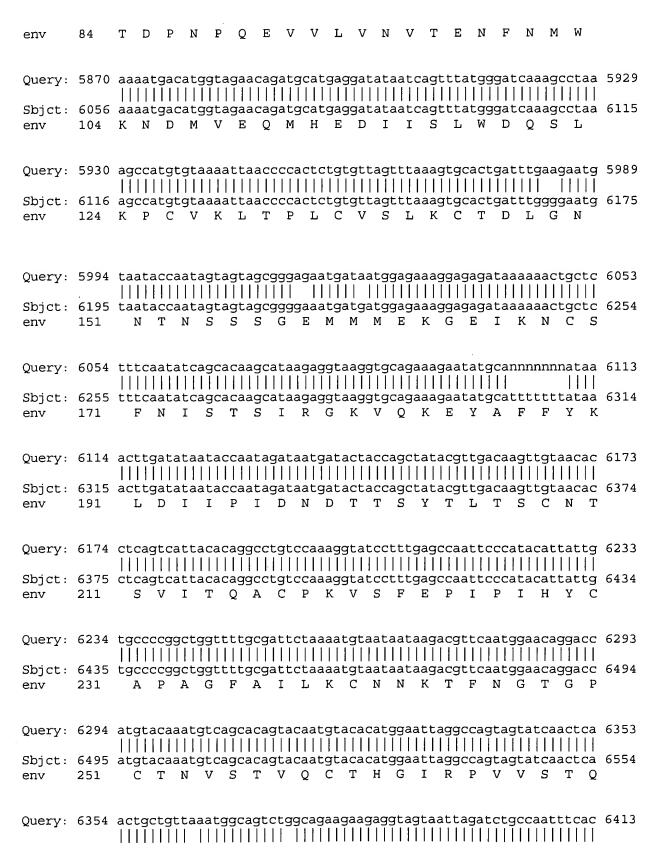
The alignment of the Query HIV sequences of Chang and the subject sequences of the present application in the region between nucleotides 4000 and 9000 are presented below.

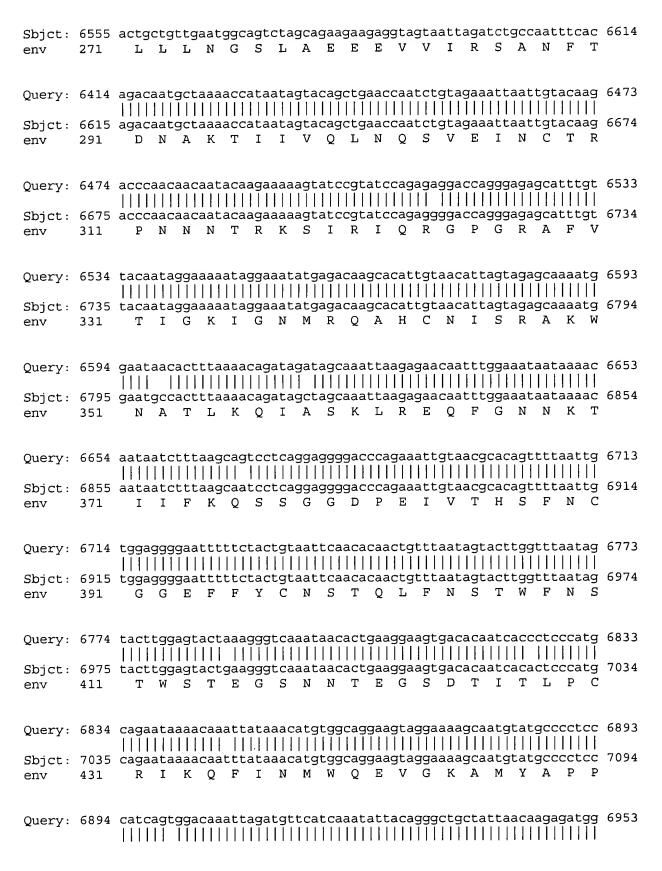
Query: 4070 ttataggacaggtaagagtcaggctgaacatcttaagacagcagtacaaatggcagtat 4129

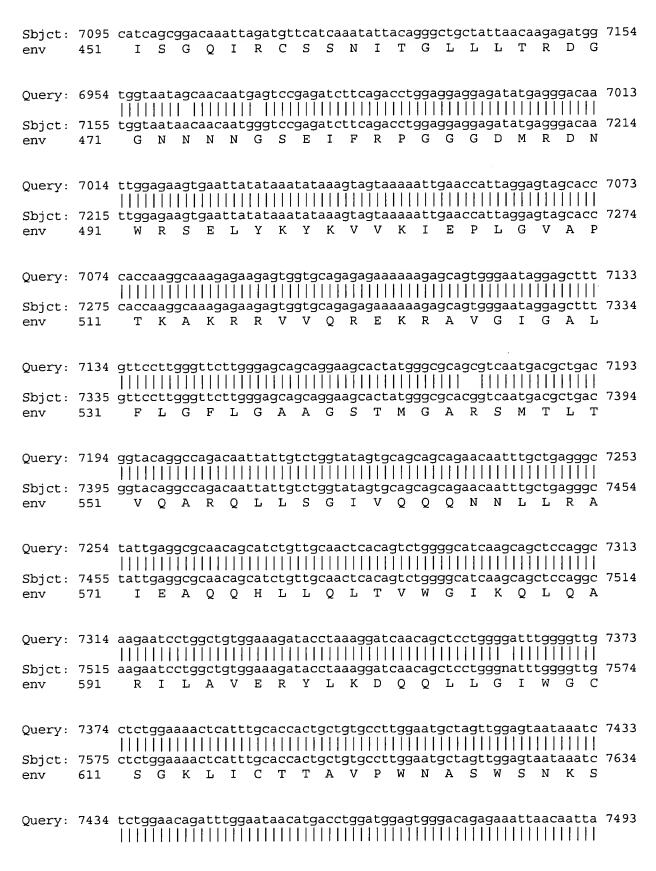


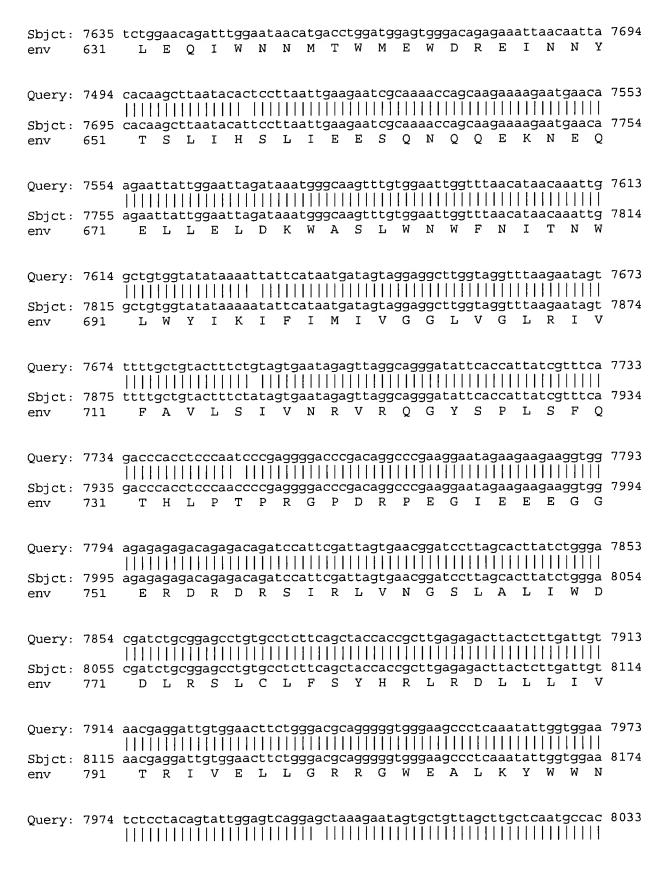
_	4670 aaaaagagatatagcacacaagtagaccctgaactagcagaccaactaattcatctgta 	
_	4730 tactttgactgtttttcagactctgctataagaaaggccttattaggacacatagttag 	
	4790 cctaggtgtgaatatcaagcaggacataacaaggtaggatctctacaatacttggcact 	
	4850 gcagcattaataacaccaaaaaagataaagccacctttgcctagtgttacgaaactgac 	
_	4910 gaggatagatggaacaagccccagaagaccaagggccacagagggagccacacaatgaa 	
	4970 ggacactagagcttttagaggagcttaagaatgaagctgttagacattttcctaggatt	
_	5030 ggctccatggcttagggcaacatatctatgaaacttatggggatacttgggcaggagtg 	
	5090 aagccataataagaattctgcaacaactgctgtttatccattttcagaattgggtgtcg 	
	5150 catagcagaataggcgttactcgacagaggagagcaagaaatggagccagtagatccta 	
	5210 actagagccctggaagcatccaggaagtcagcctaaaactgcttgtaccaattgctatt	1
Query:	5270 taaaaagtgttgctttcattgccaagtttgtttcataacaaaagccttaggcatctcct	

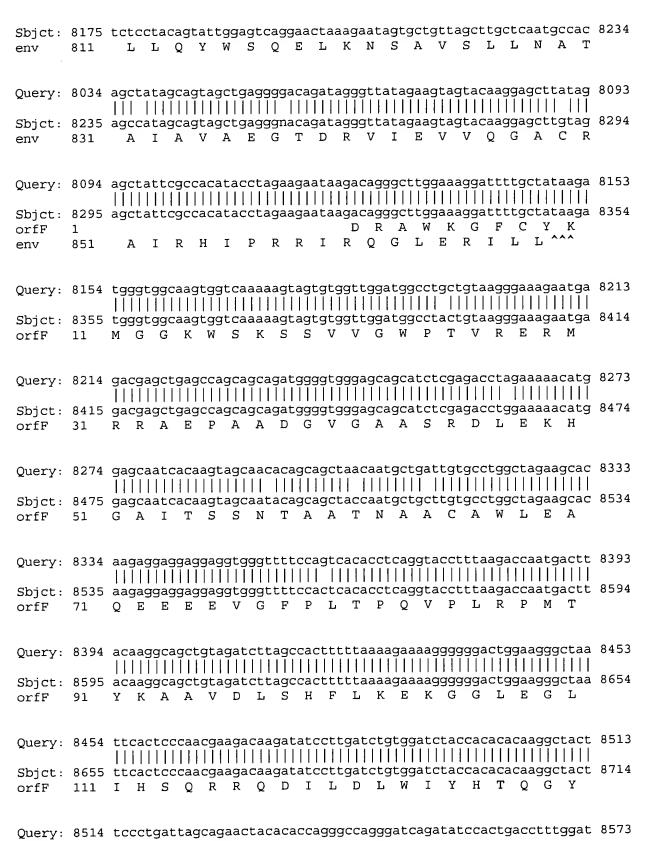












Page 12

Application/Control Number: 08/475,822

Art Unit: 1634

```
Sbjct: 8715 tccctgattggcagaactacacaccagggccaggggtcagatatccactgacctttggat 8774
    131 F P D W O N Y T P G P G V R Y P L T F G
Query: 8574 ggtgctacaagctagtaccagttgagccagagaagttagaagaagccaacaaaggagaga 8633
       Sbjct: 8775 ggtgctacaagctagtaccagttgagccagataaggtagaagaggccaataaaggagaga 8834
    151 W C Y K L V P V E P D K V E E A N K G E
orfF
171 N T S L L H P V S L H G M D D P E R E V
orfF
Query: 8694 tagagtggaggtttgacagccgcctagcatttcatcacatggcccgagagctgcatccgg 8753
       Sbjct: 8895 tagagtggaggtttgacagccgcctagcatttcatcacgtggcccgagagctgcatccgg 8954
    191 LEWRFDSRLAFHHVARELHP
orfF
Query: 8754 agtacttcaagaactgctgacatcgagcttgctacaagggactttccgctggggactttc 8813
       Sbjct: 8955 agtacttcaagaactgctgacatcgagcttgctacaagggactttccgctggggactttc 9014
    211 E Y F K N C ^^^
Query: 8814 cagggaggcgtggcctgggcgggactggggagtggcgagccctcagatcctgcatataag 8873
       Sbjct: 9015 cagggaggcgtggcctggcgggactggggagtggcgagccctcagatgctgcatataan 9074
Query: 8874 cagctgctttttgcctgtactgggtctctctggttagaccagatctgagcctgggagctc 8933
       Sbjct: 9075 cagctgcttttttgcctgtactgggtctctctggttagaccagatttgagcctgggagctc 9134
Score = 2796 bits (1454), Expect = 0.0
Identities = 1477/1489 (99%)
Strand = Plus / Plus
```

It is noted that with regard to, for example, the sequence region between nucleotides 4487 and 5086 claimed in claim 11, there are two nucleotide differences between the sequences. It is noted that the art recognizes that sequencing errors occur in a range between 0.3 % and 2.5%, as evidenced by Richterich (Genome Research (1998) 8:251-259). However, these error rates are determined using technology that

Art Unit: 1634

was significantly more advanced than that in 1984, when sequencing error rates were likely significantly higher. In the 599 nucleotide sequence which is the first sequence of claim 1, two errors would represent approximately a 0.3% error rate. Thus, these sequences are identical within the error range available and the anticipation rejection is proper.

With regard to the kit claims, it is noted that the preamble phrase "a kit" imposes no structural requirements upon the product claims.

Claim Rejections - 35 USC § 103

- 5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
 - (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
- 6. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:
 - 1. Determining the scope and contents of the prior art.
 - 2. Ascertaining the differences between the prior art and the claims at issue.
 - 3. Resolving the level of ordinary skill in the pertinent art.
 - 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
- 7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

Art Unit: 1634

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 35-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chang et al (U.S. Patent 6,001,977) as applied to claims 35, 37, 39, 41, 43 and 45 as discussed above and further in view of White et al (U.S. Patent 4,677,054).

Chang teaches the limitations of claims 35, 37, 39, 41, 43 and 45 as discussed above, including detection of HIV-1 using nucleic acid probes by dot blotting.

Chang does not teach the use of labels on the probes.

White teaches labeling probes and hybridization reagents using radioactive labels for detection of nucleic acids including RNA from animal tissue by hybridization (column 2, lines 6-34).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the method of White with the method of Change because White states that the method is widely applicable, stating "It will be obvious to those skilled in the art that the method of the present invention is general in scope and can be used for DNA and mRNA-like analysis of all sorts of biological specimens (column 2, lines 40-44)." Further motivation to detect using these methods is provided by White, who notes "Very small amounts of sample can be tested. Furthermore, the samples can be hybridized with multiple probes used in sequence (column 3, lines 2-4)". An ordinary practitioner would have been motivated to use the

. . . .

Art Unit: 1634

labels of White to detect HIV as taught by Chang since White says that the method is broadly applicable, permits the use of small sample amounts and permits detection using multiple different probes to enhance specificity.

Response to Arguments

9. Applicant's arguments filed November 19, 2003 have been fully considered but they are not persuasive.

Applicant argues that the sequence of Chang was more carefully performed than the raw sequence analysis of Richterich, because the sequence was "polished". This refers to a term of art in which the sequence is repeatedly checked for accuracy. However, the issue in the current case is simply one of fact. Are the sequences the same or not? The examiner has read portions of John Crewdson's book "Science Fictions", which discusses the original studies on HIV in 1984. Crewdson quotes Wong-Staal, a coinventor on the Chang patent, as saying "that LAV and HTLV-3 are independent isolations of the same virus (see page 165)." Crewdson further notes "They had come from the same patient (see page 165)."

Further, Applicant specifically argues that Chang performed careful analysis.

This is entirely belied and contradicted by Crewdson, who notes "The gene map of ARV, decoded by Paul Luciw and his California team, was a dead match for LAV, which meant Gallo's map was dead wrong (see page 173)." So contrary to Applicant's arguments, there was not significant care taken by Chang's group. At note s, on page 565, Crewdson writes, "The Gallo group had sequenced two clones of HTLV-3B. The first didn't appear to have the fifth gene but the second did. Or did it? Because HTLV-1

Art Unit: 1634

didn't have five genes, the prevailing opinion in Gallo's lab was that the AIDS virus didn't either and what looked like a fifth gene was an artifact." This further supports erroneous sequencing by Gallo, since at least once they failed to find an entire gene. This would be rather difficult to explain in a careful sequencing project.

So Applicant's entire argument rests on the supposition, without evidence, that the sequences were carefully performed.

Applicant's other argument is that Ratner resequences BH10. This is not correct. In reading Ratner's paper, there is no evidence that Ratner resequenced BH-10. Ratner simply compared a different clone to BH-10. At page 63, bottom of the page, Ratner states "The previously sequenced clone BH10 (28)", referring to reference 28, which is the original 1985 Nature paper and not some later resequencing. So, in fact, Ratner does NOT support applicant's position.

As a final point, it is noted that in this case, there is better evidence than is ordinarily available that the strains sequenced by the two different groups are, in fact, the same since it is clear that the LAI strain is common to both of these applications. There is express evidence, as discussed above, that the viruses were the same.

Since the evidence of record does not support Applicant's position, the rejections are maintained.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-4:00.

Page 17

Application/Control Number: 08/475,822

Art Unit: 1634

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey Fredman Primary Examiner Art Unit 1634